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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/666,696 | 09/19/2003 | Ulrich Feige | A-527H | 8548 |

7590 04/21/2006
US Patent Operations/[TJG]
Dept. 4300, M/S 27-4-A
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Thousand Oaks, CA 91320-1799

EXAMINER

WESSENDORF, TERESA D

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1639

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | | |
|------------------------------|------------------------|--|---------------------|--|
| Office Action Summary | Application No. | | Applicant(s) | |
| | 10/666,696 | | FEIGE ET AL. | |
| | Examiner | | Art Unit | |
| | T. D. Wessendorf | | 1639 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/26/2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,63 and 64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,63 and 64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Claims

Claims 1-7 and 63-64 are pending in the application and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-7 and 63-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and reiterated below.

A). The as-filed specification fails to provide a written description support for the now claimed, "randomized Ang-2 binding peptide" and "...neither X1 nor X2 is a native protein." The as-filed specification does not provide the description as to the X variables not being a native protein. MPEP 714.02 recites that applicants specifically point out where in the specification support for the new claimed limitations appear.

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B). The specification fails to provide an adequate written description of a randomized Ang-2 binding peptide molecule. The specification does not teach any peptide sequence for Ang-2 binding sequences, let alone, its randomization. There is no description as to the kind of amino acids, the location, the number of residues that can be randomized in said Ang-2 binding molecule. More importantly, the linking of said random peptide to the Fc domain. The specification provides a single statement or mention Ang-2. Other than this passing remark, no native sequence of said Ang-2 binding molecule or fragments is described, if any has been randomized. To provide adequate written description for any type of Ang-2 binding molecule linked to an Fc region by any linker, evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Response to Arguments

Applicants argue that they are not merely claiming a randomized Ang-2 binding peptide. Rather, a molecule of the formula as in claim 1 in which Ang-2 binding peptides are substituents.

In response, it is recognized that Ang-2 binding peptide is complexed with the other molecule in the formula i.e., with Fc(F1). However, even alone or with the Fc, the specification does not provide for the claimed Ang-2 binding peptide as of the filing date.

Applicants state that their invention is analogous to example 16 of the guidelines. The inventor in the Example provided a novel antigen and claimed all antibodies to the novel antigen. Here, the inventors have discovered a novel class of molecules (peptibodies) and applied that class to a known antigen (Ang-2).

In reply, the randomized Ang-2 binding peptides have been rejected under this statute because it is not described in the specification as of the filing date. It thus raises the question whether applicants are in possession of the claimed randomized Ang-2 binding peptide, at the time of the filing. Here, no peptide has been identified. Rather, a random peptide that binds

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to Ang-2 is being claimed. The peptide is described only by the claimed length and the negative limitation that it is not a native protein. There is no description as to the kind of dipeptide(2) or 40 amino acids that can comprise the peptide singly or in combination of the amino acids. The dipeptide alone could read on an innumerable numbers of amino acids, natural or synthetic, singly or in combinations. This is made more complex since the specification as of the filing date does not describe a single peptide, let alone a randomized Ang-2 binding peptide. Thus, Example 16 of the guidelines is not analogous to the instant claim compound. Except for the single statement (passing remark) made in the instant specification regarding Ang-2 binding peptide, there is no complete disclosure as to this randomized Ang-2 binding peptide i.e., peptide that are modified in every conceivable manner. The disclosure, at the time of filing, describes compounds that are remotely structurally related to randomized Ang-2 Binding peptide.

Claim Rejections - 35 USC § 103

Claims 1-7 and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti et al (WO 00/75323) and reiterated below.

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Cerretti et al discloses at page 6, lines 10-15 a Tek multimer including dimers, trimers or higher multimers covalently or non-covalently linked by peptide linkers to a Fc domain. Cerretti further discloses at page 8, line 4 up to page 9 line 6 Tek multimer variants that has one to ten amino acid sequence variations by deletions, substitutions or insertions compared to the native Tek. Furthermore, Cerretti discloses at page 14, lines 15-24 antibodies immunoreactive with the polypeptide. The Tek antibodies are prepared by phage display, inter alia. In Example 4, page 22 Cerretti describes the binding of the Tek polypeptide to the different Ang ligands, e.g., Ang-2 ligand. Cerretti discloses at page 9, lines 35-36 disclose that due to the degeneracy of genetic code, there can be considerable variation in nucleotide sequences encoding the same amino acid. Cerretti does not disclose a fusion protein of Fc wherein the Ang-2 binding is randomized. However, such randomization would have been obvious to one having ordinary skill in the art in view of the teachings of Cerretti of variants of the Ang-2 binding peptide i.e., Tek polypeptide, wherein one to ten amino acids are varied in a random manner. Such variations in the amino acids would suggest random amino acids. One having ordinary skill in

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the art would be motivated to randomized portions of the Ang-2 binding molecule (i.e., Tek). Randomization produces a diverse or more variants that leads to the discovery of lead compounds with better pharmacological effect.

Response to Arguments

Applicants state that Cerretti has been interpreted as having been withdrawn from the Advisory Action.

In response, the advisory action clearly referred to all of the rejections in the 5/4/2005 office action which have been maintained. However, the arguments have been directed only to the 35 USC 112 rejection. This does not imply that the prior art rejection has been dropped.

Applicants reiterate the arguments they made in the response to the final office action. The degeneracy of the genetic code, as cited in the prior office action, by definition refers to nucleic acids encoding the same polypeptide sequence. See Lewin, Genes IV Oxford: Oxford University Press, 1990 (enclosure sent with the response to the final office action). Thus, the mention of degenerate code by Cerretti et al. provides no teaching whatsoever regarding randomized ang-2 binding peptides. Furthermore, Cerretti et al. discuss antibodies to

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tek, with no suggestion whatsoever regarding antibodies or peptibodies binding to Ang-2.

In reply, the response made in the Final Office action is also incorporated herein. Lewin defines degeneracy as to the many changes in the codon. This many changes would read on randomized peptide. Furthermore, the nucleic acid taught by Cerretti encodes polypeptide(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-7 and 63-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Oliner et al (USA 20030236193) and repeated below.

Oliner describes at paragraph [0027] a composition comprising Fc and of a random peptides that bind to Ang-2 comprising the sequence or formula as recited therein. In another embodiment, the invention relates to a polypeptide capable of binding Ang-2 comprising an amino acid sequence of the formula: a1-a2-a3-Ca -5WDPWTC-a12-a13-a14 (SEQ ID NO: 69) wherein each of the amino acids are defined at paragraphs [0028]-[0041]. In

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paragraph [0070] the composition is specifically described.

Accordingly, the specific composition of Oliner describing the specific amino acids in the peptide sequence of the composition anticipates the broad claimed composition. [Note applicants are not entitled to the priority date of 10/23/1998 since the provisional application does not describe randomized Ang-2 binding peptide. Neither does the present application having a filing date of 9/19/2003.]

Response to Arguments

Applicants state that Oliner(U.S. Pat. App. 20030236193) application post-dates the subject application. The earliest claimed priority of Oliner et al. is to U.S. Provisional Application Serial No. 60/328,624, filed Oct. 11, 2001. That date is after all of the applications from which the present application claims priority.

In reply, since the instant claimed is not supported in the as-filed specification, hence, Oliner is a proper prior art. Applicants have not shown where in the instant and provisional application, dated 10/23/1998, the instant claim is supported to be entitled to said priority date of 1998.

No claim is allowed.

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

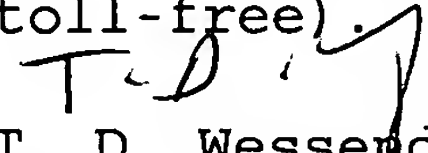
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw

April 14, 2006